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### ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31762

**Title:** A APAP-induced model of acute liver failure in pigs treated by artificial liver system

**Reviewer's code:** 01221925

**Reviewer's country:** Greece

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:50

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This is an interesting paper examining a porcine model of acetaminophen induced acute liver failure and evaluating the effect of a bioartificial liver support system. Could the authors please respond to the following comments/questions: 1) Did the authors measure APAP levels in the two groups? 2) Can the authors please describe the bioartificial liver support system used? 3) Why were there 11 pigs in the control group and 5 in the experimental one?

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31762

**Title:** A APAP-induced model of acute liver failure in pigs treated by artificial liver system

**Reviewer's code:** 01568246

**Reviewer's country:** Norway

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-12-06 21:50

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The aim of the present study was to develop a procedure for acetaminophen (APAP)-induced acute liver failure (ALF) in pigs, and to design methods for treating the ALF by means of an artificial liver system. Methods for APAP induced ALF have been presented earlier, the purpose of the present paper was to improve the previously published methods. The model presented for following the development of an acute liver failure induced by APAP in mini-pigs seems to be based on reliable and adequate methods. The model seems to satisfy the criteria suggested by Terblanche and Hickman (reference number 8). The manuscript raises, however, several questions that need to be dealt with: 1. The aim of the work was to establish a highly reversible porcine model of ALF and treat it with an artificial liver system. It is easy to see that the work has led to a model of ALF. However, although referred to several times, an artificial liver system has not been described in the paper. This is very unexpected as the results indicate clearly that an artificial liver support system has been used with very good effect. 2. The method for the development of ALF was to treat the animals with APAP. The data obtained were the result of one experiment with 11 animals. In the treatment with APAP

only one time period and only one concentration of the main parameter were tested. It may therefore be too optimistic to state that the model is highly reversible. 3. According to ?Biochemical index assessment? blood samples were collected at regular intervals (every 2 hours). It would be interesting to see in more detail the time course for the blood concentrations of the selected biochemical parameters. The authors evidently have the data needed. 4. Sixteen pigs were used, 11 experimental and 6 control animals. One would expect that the treatment of the controls should be the same as for the experimental animals except that the controls should not be given APAP. Nevertheless, after 20 hours of treatment of the experimental animals with APAP the serum biochemical parameters are approximately equal in experimental and control animals. The authors have not discussed this unexpected finding. 5. The description of the appearance/morphology of the livers are not very precise and the microscopical histological observations do not give much information about parenchymal and sinusoidal liver cells. Even the control livers showed very abnormal morphology. According to Materials and Methods both light and electron microscopy were used. Very important information about the effects of APAP would conceivably be obtained if the authors could present high quality pictures obtained by light and electron microscopy. Minor points: 1. The survival curve for treatment and control groups in Figure 1 is not easy to understand when reading the text in chapter ?End of study in treatment and controls?. Here one reads that control animals were sacrificed with pentobarbital. (2) The paper reads well although some misprints need to be corrected. For instance in Abstract is written: ?ammonia were showed a decrease..? should read: ammonia showed a decrease. (3) Core tip: Where in the manuscript is the actual bioartificial liver described in detail? The first sentences in this section (Core tip) should be rewritten. (4) In Materials and Methods under ?Supportive care? amounts are given as percentage, This information should be more precise (weights/volume).